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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 09/935,316 | 08/22/2001 | Ching-Leou Teng | ISIS-4824 | 1463 |

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| EXAMINER | |
|---|---|
| ANGELL, JON E | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1635 | |

DATE MAILED: 11/27/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/935,316 | TENG ET AL. | |
| | Examiner | Art Unit | |
| | Jon Eric Angell | 1635 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *18 July 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *30-42* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *30-42* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *22 August 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

### *Continued Examination Under 37 CFR 1.114*

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 7/18/2006 has been entered.

Applicant's arguments are addressed on a per section basis. The text of those sections of Title 35, U.S. Code not included in this Action can be found in a prior Office Action. Any rejections not reiterated in this action have been withdrawn as being obviated by the amendment of the claims and/or applicant's arguments.

Claims 30-42 are currently pending and are addressed herein.

### *Claim Rejections - 35 USC § 112*

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 30-42 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant

art that the inventor(s), at the time the application was filed, had possession of the claimed invention. **This is a new matter rejection.**

37 CFR 1.118 (a) states that "No amendment shall introduce new matter into the disclosure of an application after the filing date of the application".

MPEP §2163.06 notes:

If new matter is added to the claims, the examiner should reject the claims under 35 U.S.C. 112, first paragraph - written description requirement. In re Rasmussen, 650 F.2d 1212, 211 USPQ 323 (CCPA 1981).

MPEP §2163.02 teaches that:

Whenever the issue arises, the fundamental factual inquiry is whether a claim defines an invention that is clearly conveyed to those skilled in the art at the time the application was filed...If a claim is amended to include subject matter, limitations, or terminology not present in the application as filed, involving a departure from, addition to, or deletion from the disclosure of the application as filed, the examiner should conclude that the claimed subject matter is not described in that application.

MPEP §2163.06 further notes:

When an amendment is filed in reply to an objection or rejection based on 35 U.S.C. 112, first paragraph, a study of the entire application is often necessary to determine whether or not "new matter" is involved. Applicant should therefore specifically point out the support for any amendments made to the disclosure.

In the instant case, claim 30 has been amended to include the new limitation that the first population and second population of carrier particles are administered in a single pharmaceutical formulation in a single compartment capsule (Emphasis added). Claim 40 has been amended to include the new limitation that the first population and second population of carrier particles are administered in a single pharmaceutical formulation and said first population and second population of carrier particles are released concurrently to said intestine tissue in a single compartment capsule. Applicants have pointed to paragraph 0124 of the specification as support

for the limitation "single compartment capsule". Paragraph 0124, was closely reviewed by the Examiner, however, neither explicit, implicit nor inherent support for a "single compartment capsule" was found in paragraph 0124, or anywhere else in the specification.

Specifically, paragraph 0124 states:

> Capsules used for oral delivery may include formulations that are well known in the art. Further, multicompartment hard capsules with control release properties as described by Digenis et al., U.S. Pat. No. 5,672,359, and water permeable capsules with a multi-stage drug delivery system as described by Amidon et al., U.S. Pat. No. 5,674,530 may also be used to formulate the compositions of the present invention.

Certainly paragraph 0124 does not have explicit support for a single compartment capsule. Furthermore, at best, paragraph 0124 indicates that capsules can be any of a genus of formulations that are well known in the art, specifically including two species: multicompartment hard capsules and water permeable capsules. Therefore, the paragraph 0124 has contemplated using a broad genus of capsules and has further explicilty disclosed two species of that broad genus. Paragraph 0124 does not contemplate using the species which is a single compartment capsule. Since the disclosure of a broad genus does not anticipate every species which it encompasses, the disclosure of paragraph 0124 does provide proper support for a single compartment capsule.

Applicants are respectfully reminded that MPEP 2163.05 II states:

> The introduction of claim changes which involve narrowing the claims by introducing elements or limitations which are not supported by the as-filed disclosure is a violation of the written description requirement of 35 U.S.C. 112, first paragraph. See, e.g., Fujikawa v. Wattanasin, 93 F.3d 1559, 1571, 39 USPQ2d 1895, 1905 (Fed. Cir. 1996) (a "laundry list" disclosure of every possible moiety does not constitute a written description of every species in a genus because it would not "reasonably lead" those skilled in the art to any particular species); In re Ruschig, 379 F.2d 990, 995, 154 USPQ 118, 123 (CCPA 1967)... See also In re Smith, 458 F.2d 1389, 1395, 173 USPQ 679, 683 (CCPA 1972) ("Whatever may be the viability of an inductive-deductive approach to arriving at a

> claimed subgenus, it cannot be said that such a subgenus is necessarily described by a genus encompassing it and a species upon which it reads."...

Therefore, the new limitation "single compartment capsule" is new matter and a rejection under 35 U.S.C. 112, first paragraph is proper. Claims 31-39, 41 and 42 are rejected because they are dependent claims which encompass all of the limitations of the claims from which they depend, including the new matter limitation.

To the extent that the claimed compositions and/or methods are not described in the instant disclosure, the instant claims are also rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention, since a disclosure cannot teach one to make or use something that has not been described.

***Claim Rejections - 35 USC § 102***

1. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

2. Claims 30-36, 38-42 are rejected under 35 U.S.C. 102(b) as being anticipated by US Patent 5,877,309 (McKay et al.)

The instant claims are drawn to:

A method for enhancing the intestinal absorption of a drug in an animal, said method comprising administering to the animal:

(a) a first population of carrier particles comprising a drug-bioadhesive component; and,

(b) a second population of carrier particles comprising a penetration enhancer,

wherein intestinal tissue is activated by said penetration enhancer prior to the arrival of said drug and said first population and second population of carrier particles are administered in a single pharmaceutical composition in a single compartment capsule (claim 30); wherein the first population is prepared as a tablet or a multiparticulate formulation (claim 31); wherein the second population is prepared as a tablet, multiparticulate, emulsion microemulsion, or self-emulsifying system (claim 32); wherein the drug is an oligonucleotide (claim 33); wherein the penetration enhancer is a fatty acid (claim 34); wherein a bioadhesive of the drug-bioadhesive is a polyacrylic polymer (claim 35); and wherein the oligonucleotide is an antisense oligonucleotide (claim 36); wherein the bioadhesive comprises a polyacrylic polymer (claim 38); wherein the bioadhesive further comprises a hydroxypropyl-methylcellulose (HPMC) (claim 39); and wherein the capsule is not a multicompartment capsule (claim 41); and,

A method for enhancing the intestinal absorption of a drug in an animal, said method comprising administering to the animal:

(a) a first population of carrier particles comprising a drug-bioadhesive component; and,

(b) a second population of carrier particles comprising a penetration enhancer,

wherein intestinal tissue is activated by said penetration enhancer prior to the arrival of said drug and said first population and second population of carrier particles are administered in a single pharmaceutical formulation and wherein the first population and second population of particles are released concurrently to said intestinal tissue (claim 40); wherein the capsule is not a multicompartment capsule (claim 42).

McKay teaches a method which comprises administering to a human a composition comprising a drug that is an antisense oligonucleotide (e.g., column 6, lines 29-65); wherein the antisense oligonucleotide is comprised in a formulation for oral delivery which can comprise a polyacrylic polymer, such as capric acid and polyacrylates (e.g., see: col. 20, lines 52-54; col.22, lines 4-19; col. 23, lines 24-40; col. 25, lines 1-7; and col. 28, lines 3-4). McKay teaches that the therapeutic formulation can be comprised in a capsule or tablet, which as described by McKay would be a single compartment capsule (e.g., see column 22, lines 49-60). Furthermore, McKay does not indicate that the capsules or tablets can be multicompartment capsules. Additionally, McKay teaches that the antisense drug composition can comprise hydroxypropylmethylcellulose and polyacrylates (e.g., see col. 23, lines 29-40).

Therefore, McKay teaches a method comprising administering to a subject a composition comprising all of structural elements of instant claims. Therefore, the method taught by McKay, absent evidence to the contrary, would necessarily have the same result as the instant claimed method.

***Claim Rejections - 35 USC § 103***

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

4. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

5. Claims 30, 33 and 37 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent 5,877,309 (McKay et al.), further in view of US Patent 5,514,788 (Bennett et al.).

It is noted that McKay teaches a method for enhancing the intestinal absorption of an antisense drug in an animal, comprising administering to the animal a formulation comprising: (a) a first population of carrier particles comprising an drug-bioadhesive component, wherein the drug is an antisense oligonucleotide; and (b) a second population of carrier particles comprising a penetration enhancer, as indicated above.

McKay does not teach that the oligonucleotide comprises SEQ ID NO: 1 (claim 37).

However, Bennett teaches an antisense oligonucleotide that exactly matches SEQ ID NO: 1 of the instant claims (see SEQ ID NO: 22 in column 35 of Bennett) wherein the antisense oligonucleotide can be used administered to an animal for a method of treatment (e.g., see abstract).

Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of McKay and Bennet to make a method comprising administering to an animal a composition comprising (a) a first population of carrier particles comprising an drug-bioadhesive component, wherein the drug is an antisense oligonucleotide comprising the antisense oligonucleotide taught by Bennet; and (b) a second population of carrier particles comprising a penetration enhancer, with a reasonable expectation of success.

The motivation to make the modification is provide in part by both McKay and Bennett. Specifically, McKay teaches a method for administering a therapeutic antisense oligonucleotide to an animal and Bennett teaches a specific therapeutic antisense oligonucleotide comprising SEQ ID NO: 1.

***Claim Objections***

Claims 41 and 42 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form.

***Response to Arguments***

Applicant's arguments filed 7/18/2006 have been fully considered but they are not persuasive.

Applicants argue that support for a "single compartment capsule" can be found in paragraph 0124 because the existence of single compartment capsules (i.e., non-multicompartment capsules) is implicit and inherent by the distinction that the capsules may be "multicompartment capsules". Applicants assert that if only multicompartment capsules were known, such a modifier would not be required.

In response, paragraph 0124 states:

> Capsules used for oral delivery may include formulations that are well known in the art. Further, multicompartment hard capsules with control release properties as described by Digenis et al., U.S. Pat. No. 5,672,359, and water permeable capsules with a multi-stage drug delivery system as described by Amidon et al., U.S. Pat. No. 5,674,530 may also be used to formulate the compositions of the present invention.

Certainly paragraph 0124 does not have explicit support for a single compartment capsule. Furthermore, at best, paragraph 0124 indicates that capsules can be any of a genus of formulations that are well known in the art, specifically including two species: multicompartment hard capsules and water permeable capsules. Therefore, the paragraph 0124 has contemplated using a broad genus of capsules and has further explicilty disclosed two species of that broad genus. Paragraph 0124 does not contemplate using the species which is a single compartment capsule.. Since the disclosure of a broad genus does not anticipate every species which it encompasses, the disclosure of paragraph 0124 does provide proper support for a single compartment capsule. Applicants argument that "the existence of single compartment capsules (i.e., non-multicompartment capsules) is implicit and inherent by the distinction that the

capsules may be "multicompartment capsules" is not persuasive. Applicants appear to be arguing that paragraph 0124 discloses using capsules, specifically indentifying "mutlicompartment capsules" as one type of capsule which can be used, which, according to applicants, should be taken as implicitly and inherently disclosing the use of single compartment capsules. However, paragraph 0124 discloses "multicompartment **hard** capsules" (emphasis added) which is different from "multicompartment capsules" as indicated by Applicants. Therefore, paragraph 0124 has no more support for the species "single compartment capsule" than it does for the species "mutlicompartment non-hard capsule".

Applicants also argue that single compartment capsules are well known to those of skill in the art at the time of filing.

In response, 37 CFR 1.118 (a) states that "No amendment shall introduce new matter into the disclosure of an application after the filing date of the application". Therefore, regardless of what was known by one of skill in the art at the time of filing, the amendment introducing new matter into the claims is prohibited.

Applicants also argue that the Examiner has not provided sufficient evidence to indicate that they were not in possession of the now claimed invention at the time of filing.

In response, the issue here is that Applicants have added a limitation which changes the scope of the claims in order to overcome a rejection under 35 U.S.C. 103(a). Analysis of the original disclosure reveals that the specification does not explicitly, inherently or implicitly

disclose what is now claimed. Therefore, a rejection under 35 U.S.C. 112, first paragraph is proper.

Therefore, applicants arguments are not persuasive.

***Conclusion***

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jon Eric Angell whose telephone number is 571-272-0756. The examiner can normally be reached on 9:00 a.m.- 5:00 p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Douglas Schultz can be reached on 571-272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

JEA

JON E. ANGELL, PH.D.
PRIMARY EXAMINER